

What we claim is:

Sub C1

1. A transgenic non-human mammal containing an exogenous DNA sequence stably integrated in its genome, wherein said exogenous DNA sequence comprises substantially the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene, or a variant thereof, operably linked to a DNA sequence encoding a polypeptide having protein C activity and a signal peptide, wherein said whey acidic protein promoter is specifically active in mammary cells and said signal peptide is effective in directing the secretion of said polypeptide into the milk of said transgenic mammal.

2. The transgenic non-human mammal of claim 1, wherein said DNA sequence encoding a polypeptide having human protein C activity comprises portions of the non-coding regions of the human protein C gene.

3. The transgenic non-human mammal of claim 1, wherein said DNA sequence encoding a polypeptide having human protein C activity comprises substantially the human protein C gene from 21 basepairs upstream of the protein C start codon to the *NheI* site in the 3' end of the protein C gene, or a variant thereof.

Sub. 102

4. The transgenic non-human mammal of claim 1, wherein said exogenous DNA sequence comprises a DNA sequence consisting essentially of the 5' 4.2 kb *Sau3A* - *Kpn1* promoter fragment of the mouse whey

Sub. 52

acidic protein promoter ligated directly or by a linker to a fragment of the human protein C gene beginning 21 basepairs upstream of the protein C start codon and ending at the *NheI* site in the 3' end of the protein C gene.

5. The transgenic non-human mammal of claim 4, wherein said mammal is mouse, pig, goat, or sheep.

Sub. C2

6. A process for the production of protein C, comprising the steps of

(A) providing a non-human transgenic mammal characterized by an exogenous DNA sequence stably integrated in its genome, wherein said exogenous DNA sequence comprises substantially the 5' 4.2 kb *Sau3A* - *KpnI* promoter of the mouse whey acidic protein gene, or a variant thereof, operably linked to a DNA sequence encoding a polypeptide having protein C activity and a signal peptide, said promoter being specifically active in mammary cells and said signal peptide being effective in directing the secretion of said polypeptide into the milk of said transgenic mammal;

(B) producing milk from said transgenic mammal;

(C) collecting said milk; and

(D) isolating said polypeptide from said milk.

7. The process of claim 6, wherein said DNA sequence encoding a polypeptide having human protein

Plc 2  
C activity comprises portions of the non-coding regions of the human protein C gene.

8. The process of claim 6, wherein said DNA sequence encoding a polypeptide having human protein C activity comprises the human protein C gene from 21 basepairs upstream of the protein C start codon to the *NheI* site in the 3' end of the protein C gene.

Sub. 14  
~~9. The process of claim 6, wherein said exogenous DNA comprises a DNA sequence consisting essentially of the 5' 4.2 kb *Sau3A* - *Kpn1* promoter fragment of the mouse whey acidic protein promoter ligated directly or by a linker to a fragment of the human protein C gene beginning 21 basepairs upstream of the protein C start codon and ending at the *NheI* site in the 3' end of the protein C gene.~~

10. The transgenic non-human mammal of claim 9, wherein said mammal is mouse, pig, goat or sheep.

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Plc 3  
11. A process for producing <sup>non-human</sup> transgenic animals, comprising the steps of (A) providing a mixture containing a double-stranded DNA; (B) subjecting said mixture to anion-exchange high performance liquid chromatography to obtain purified double-stranded DNA; and thereafter (C) microinjecting an aqueous buffer solution containing said purified double-stranded DNA into an animal embryo, wherein said double-stranded DNA is selected from the group consisting of a double-stranded DNA comprising substantially the 5' 4.2 kb *Sau3A* - *Kpn1*

D3  
P3  
P3

promoter fragment of the mouse whey acidic protein promoter, a double-stranded DNA comprising substantially a fragment of the human protein C gene beginning 21 basepairs upstream of the protein C start codon and ending at the *NheI* site in the 3' end of the protein C gene, and a double-stranded DNA comprising a DNA sequence consisting essentially of the 5' 4.2 kb *Sau3A* - *Kpn1* promoter fragment of the mouse whey acidic protein promoter ligated directly or by a linker to a fragment of the human protein C gene beginning 21 basepairs upstream of the protein C start codon and ending at the *NheI* site in the 3' end of the protein C gene.

12. A process for the production of a polypeptide in the milk of a transgenic non-human mammal, comprising the steps of:

(A) providing a non-human transgenic mammal characterized by an exogenous DNA sequence stably integrated in its genome, wherein said exogenous DNA sequence comprises substantially the 5' 4.2 kb *Sau3A* - *Kpn1* promoter of the mouse whey acidic protein gene, or a variant thereof, operably linked to a DNA sequence encoding said polypeptide and a signal peptide, said promoter being specifically active in mammary cells and said signal peptide being effective in directing the secretion of said polypeptide into the milk of said transgenic mammal;

(B) producing milk from said transgenic mammal;

(C) collecting said milk; and

(D) isolating said polypeptide from said milk.

13. The process of claim 12, wherein said transgenic non-human mammal is mouse, pig, goat or sheep.

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C  
14. A transgenic non-human mammal containing an exogenous DNA sequence stably integrated in its genome, wherein said exogenous DNA sequence comprises substantially the 5' 4.2 kb *Sau3A* - *Kpn1* promoter fragment of the mouse whey acidic protein promoter, or a variant thereof operably linked to a DNA encoding a polypeptide whereby said protein is expressed specifically in mammary cells of said transgenic mammal and said protein comprises a signal peptide, said peptide being effective in directing the secretion of said protein into the milk of said mammal.

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B  
15. The transgenic non-human mammal of claim 14, wherein said mammal is mouse, pig, goat or sheep.

add CS  
Mol  
E'